



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,369	04/11/2006	Marco Alexander Van Den Berg	4662-168	9073

23117 7590 10/26/2010
NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER

ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
----------	--------------

1652

MAIL DATE	DELIVERY MODE
-----------	---------------

10/26/2010

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/575,369	Applicant(s) VAN DEN BERG, MARCO ALEXANDER	
	Examiner HOPE A. ROBINSON	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 August 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-20 and 27-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-20 and 27-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
- 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
- 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

1. Applicant's response to the Office Action mailed August 13, 2010 on May 13, 2010 is acknowledged.

Claim Disposition

2. Claims 15-20 and 27-37 are pending and are under examination based on the rejoinder of claims in the Petition Decision mailed November 23, 2009.

Claim Objection

3. Claims 15, 29 and 31-37 are objected to because of the following informalities:

Claim 15 is objected to because item (a) and (c) recites "a host cell/the host cell", however item (b) recites "host cells". The claim language should be amended to be consistent. In addition, the claim is objected to for the recitation of "the host cell's genome" which should be amended to recite, "the host cell genome".

Claim 29 is objected to for the recitation of "a modified host cell" in the preamble and "host cells" in the method steps. See also claims 31-37.

Correction is required.

Maintained-Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

4. Claims 15-20 and 27-38 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter, which applicant (s) regard as their invention.

Claims 15 and 29 as amended recites, “transfecting a host cell with an expression cassette which is covalently coupled to a fluorescent label”. The instant specification at paragraphs [0041-0042] disclose that the plasmid pGBDEL4L containing an expression cassette to drive expression, said plasmid labeled with a fluorescent label was transfected into *Penicillium chrysogenum* cells, thus the metes and bounds of the claim is unclear. The dependent claims hereto are also included.

Claim 16 is indefinite for the recitation of “said DNA is involved in production of the desired metabolite” as the claims are drawn to a method thus should provide how the DNA is “involved”, therefore, the metes and bounds of the claim is undefined. The dependent claims hereto are also included.

Claim 28 is indefinite for the recitation of “wherein RNA and protein expression levels are altered in the modified host cell” as it is unclear how these are altered based on the method steps of claim 15.

Claims 30 and 35 are indefinite for the recitation of “under proliferating conditions” because neither the claims nor the specification sets forth what those conditions are. See also claim 16 that has similar language.

Claim 20 is indefinite for the recitation of an “anti-infective” as the metes and bounds of the claim is unclear/undefined.

Maintained-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 15-18, 28-30, 33-35 and 37 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolff et al. (U.S. Patent No. 6,262,252, July 17, 2001).

Wolff et al. teach a general method of covalently attaching a label to a target molecule using detectable fluorescent tags (see paragraph 4 and 15). Wolff et al. specifically teach a method for covalently attaching a fluorescent label to a nucleic acid (see claims 1-8 of the patent). Wolff et al. teach cells transfected with a DNA (see paragraph 227). In addition, Wolff et al. teach gene transfer (see paragraph 57). Wolff et al. teach means of isolation (see paragraphs 95, 105 and 107). At paragraphs 227 and 229, Wolff et al. teach that the cells are transfected with the DNA and then cultured, fixed and analyzed via a fluorescent microscopy. The cells are compared with cells with unlabeled DNA. Thus, claims reciting isolation of cells with the labeled DNA and

multiplying the cells is anticipated. Further, as protein expression occurs from the integrated DNA, it would inherently produce a metabolic change (i.e. a metabolite (amino acid)). The labels utilized by Wolff et al. are for example fluorescein, rhodamine, digoxin (see column 6 of the patent), thus would not produce an inheritable trait, especially since the instant application also utilizes fluorescein. Therefore, the limitations of the claims are met by the reference.

6. Claims 15-18, 28-30, 33-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnson et al. (AAPS Pharmsci, 1999, cited on the IDS filed January 18, 2007).

Johnson et al. teach a method for monitoring transfer of DNA during transfection, said method involving labeling a plasmid DNA with fluorescein-12-dUTP, flow cytometric detection and sorting of the fluorescent transfected cells (see pages 1-6). Therefore, the limitations of the claims are met by the reference. The reference teaches culturing the cells, sorting the cells and analyzing individual cells (see pages 2-4 of the reference). Johnson et al. utilized a fluorescein label as in the instant case thus the label would inherently not provide an inheritable trait. Further, claims reciting isolation of cells with the labeled DNA and multiplying the cells is anticipated. Further, as protein expression occurs from the integrated DNA, it would inherently produce a metabolic change (i.e. a metabolite (amino acid)). Therefore, the limitations of the claims are met by the reference.

Response to Arguments

7. Applicant's comments have been considered in full, however, are not persuasive. Note that the art rejections of record remain and have been amended. Withdrawn rejections/objections will not be discussed herein as applicant's comments are moot. Note that the rejections of record under 35 USC 112, second paragraph and 102 remains for the reasons set forth above and herein.

Regarding the rejection under 35 USC 112 second, paragraph applicant states that the language in claim 15 is definite, note that the rejection of record has been withdrawn, however, note that the amendatory language in claims 15 and 29 is rejected as the specification discloses that a plasmid containing the expression cassette is transfected. With regard to claim 16 applicants state that the amendment obviates this ground of rejection, however, the language "involved in" remains in the claim, thus the rejection remains. Further, claims 16, 30 and 35 are rejected based on the language "under conditions to", applicants state that one of ordinary skill in the art would understand what conditions. Note that the claims broadly read on any host cell, thus it is unclear what conditions would serve as generic to any host cell. Applicant states that the rejection over claim 28 is obviated with the amendments to claim 15, however, this argument is not persuasive as claim 28 does not mention what is altered and neither does independent claim 15.

Note that the art rejections of record remain under 35 USC 102. Applicant states that the Wolff nor Johnson teaches an expression cassette to provide a modified host cell. This argument is not persuasive as the instant specification indicates that a linear DNA is contained in the plasmid which contains an expression cassette, and in deed Wolff et al. teaches a labeled DNA, Wolf et al. performs isolation as the cells are sorted and analyzed with respect to the fluorescent labeled DNA cells compared to cells with non-labeled DNA (see paragraphs 227 and 229 in the Wolff et al. patent). It is also stated that Wolff et al. does not change a metabolic process, however, the patented method employs a DNA labeled with the same fluorescent label used in the patent and the claims are broadly drawn to any DNA and host cells with any label. It is also stated that the claimed invention requires stable transfection, not shown by Wolff. Moreover, selection pressure is utilized in the reference, thus the DNA would be integrated into the genome. The reference also teaches that the cells with the transfected labeled DNA is cultured and incubated (proliferating conditions). Further, the instant specification discloses at paragraph [0047] and [0045] that [T]his example demonstrates that applying directly detectable signals (in this case fluorescein) covalently coupled to DNA as a means of selecting and sorting the desired, modified cells results in cells in which the polynucleotide of interest triggers permanent metabolic changes. The results shown in table 1 demonstrate that protoplasts can resist the pressure in the FACS. Due to some clumping of protoplasts high and low scatter populations were isolated (see table 1). Only, cells with high scatter gave amdS positive clones (see sample E, table 1), demonstrating integration of fluorescent labeled DNA. So, after growing on synthetic

media these cells lost the non-inheritable fluorescein marker, but retained the gene of interest". Thus, it appears the modification in the cell is being attributed to the DNA with fluorescein. Note that the cited Wolff reference also teach the use of fluorescein coupled to a plasmid, therefore the cell is inherently modified. Thus, applicant's arguments are not persuasive.

The same reasoning is provided for the Johnson reference, at page 2, second paragraph it is disclosed that "this article describes a method for monitoring the kinetics of the transfer of exogenous DNA during transfection....this method could detect cells containing internalized DNA as early as 1 hour after transfection and provide the intracellular location of the transferred DNA" (page 2). It is also disclosed in the materials and methods, that "a plasmid was labeled with fluorescein-12-dUTP (using nick translation). Thus both references are pertinent to the claimed invention, therefore, the rejections remain.

Conclusion

8. No claims are presently allowable.
9. Applicant's amendment necessitated the new/modified ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See

MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope A. Robinson whose telephone number is 571-272-0957. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi, can be reached at (571) 272-0956.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1652

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Hope A. Robinson/

Primary Examiner, Art Unit 1652